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November 15, 2006

Mr. Charles M. Auer, Director  
Office of Pollution Prevention and Toxics (7401M)  
Ariel Rios Building  
USEPA Headquarters  
1200 Pennsylvania Ave., N.W.  
Washington, D. C. 20460

Attn: Chemical Right-to-Know Program

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**RE: HPV Chemical Challenge Program, AR-201-14949**

Dear Mr. Auer:

Thank you for your letter dated September 29, 2006, which mentioned a response about a final data package submission for 2-chloro-N-(chloromethyl)-N-(2,6-diethylphenyl)acetamide (CMA) (CAS RN: 40164-69-0) relative to the High Production Volume (HPV) Challenge Program. The letter noted that EPA had commented on the robust summaries and test plan submission, but Monsanto Company had not yet responded.

Monsanto considers the submitted test plan and robust summaries for CMA to be the final data package for the purposes of the HPV Challenge Program. Since modifications to the submission were considered to be not necessary, especially since CMA is used solely at a limited number of manufacturing sites in the final step to synthesize alachlor and other structurally similar herbicides that have been thoroughly tested to meet regulatory requirements established under FIFRA and similar provisions in other countries, it seemed that a response was not needed in order to finalize the submission.

Monsanto is impressed with the thorough review and detailed comments provided by EPA. EPA noted that the submitted data for most endpoints were adequate for the purposes of the HPV program. Monsanto also received comments from Environmental Defense (ED).

To briefly respond to the specific comments provided by EPA, Monsanto wishes to add the following information:

1. Analog Justification. EPA commented that the use of the pesticide alachlor to satisfy some endpoints was not supported because even chemicals with similar molecular structures can react differently, with the comment specifically identifying "the labile Cl- of CMA" which will react differently than alachlor with water. Monsanto agrees that CMA will react differently than alachlor with water, which is shown by the hydrolysis data. This functional group reactivity of CMA is the single chemical difference and the rationale behind the controlled process that converts all the CMA intermediate to alachlor with methanol. Sponsors were encouraged to



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provide analog data whenever possible in order to fill the purposes of the HPV Challenge Program. In fact, the main comment received from ED was, "Our review of this submission indicates CMA appears to have low potential for environmental or human exposure. Further, with the exception of high toxicity to algae (based on data bridged from alachlor) it has little environmental or mammalian acute toxicity, it is not mutagenic and it should not persist in the environment. Therefore, we are in general agreement with Monsanto that where necessary it is appropriate to bridge data from alachlor to predict properties of CMA. Thus, no additional testing of CMA should be necessary."

2. Physicochemical Properties. EPA commented that data for melting point, boiling point, and partition endpoints were adequate, and asked for additional data or explanations about vapor pressure and water solubility. Vapor pressures for both CMA and alachlor were noted in the robust summaries. The CMA vapor pressures are written as open-ended values to reflect the typical values based on material actually tested, and which may vary slightly from sample to sample, rather than guaranteeing an analysis of any specific lot or as specifications for the product. Monsanto regrets the confusion caused by the apparently contradictory statements in summaries for water solubility (unstable, reacts slowly) and stability in water (hydrolyzes extremely rapidly). As remarked in the water solubility summary, because hydrolysis is so rapid, contact between water and CMA should be prevented and is rapid enough that water solubility testing is irrelevant. As remarked in the stability in water (hydrolysis) summary, the hydrolysis of CMA leads to the rapid release of formaldehyde and hydrochloric acid and the creation of the corresponding acetanilide product, 2-chloro-N-(2,6-diethylphenyl)acetamide (CAS RN: 6967-29-9), which is also a metabolite of alachlor. Therefore, as previously mentioned, alachlor indeed becomes a reasonable analog for CMA for the purposes of the HPV Challenge Program environmental fate and other endpoints because it actually does represent the compound that becomes subject to further biodegradation in the environment and to which humans and other organisms would be exposed.
3. Environmental Fate. EPA commented that additional data would be needed for biodegradation and transport/distribution in the environment unless the confusion about the hydrolysis rate and hydrolysis products was clarified. As explained above, CMA will hydrolyze before it will biodegrade and before transport/distribution in the environment can take place. Also, the data provided in the summaries for the acetochlor intermediate of similar structure and alachlor do represent appropriate analogs for the purposes of the HPV Challenge Program.
4. Health Effects. EPA commented that data for developmental toxicity, acute toxicity, and gene mutation were adequate, and asked for additional data for assessing chromosomal aberrations, repeated-dose toxicity, and reproductive toxicity. CMA itself was the test substance used for each study referenced in the summaries, and additional data for alachlor has been submitted to EPA as a chemical analog to further bridge assessments for CMA where additional data is desired and which should be appropriate for the purposes of the HPV Challenge Program. As mentioned above, extensive testing of alachlor and similar active ingredients has been done under the strict regulatory requirements of FIFRA to evaluate these health effects endpoints. The data is too large to adequately summarize here, but electronic copies of pesticide reregistration documents and fact sheets are available at <http://www.epa.gov/REDs>. For alachlor, the EPA Reregistration Eligibility Decision (RED) fact sheet toxicity section summarizes the repeated-dose and reproductive toxicity



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data and includes the statement, "The alachlor database for pre- and post-natal effects is complete based on current requirements."

5. Ecological Effects. EPA commented that it reserved judgment on fish, aquatic invertebrate and aquatic plant endpoints until the question on the hydrolysis of CMA was clarified to determine if the nominal concentrations of CMA were maintained during the tests. As explained above, the nominal starting concentrations of CMA would not be maintained and the results should be interpreted to represent primarily exposure to the hydrolysis product. EPA also commented that a clarification about submitted alachlor data was needed to determine if test concentrations were using measured or nominal concentrations. As stated in the robust summary for algae with alachlor, "Mean measured test concentrations were determined from samples of test medium collected from each treatment and control group at the beginning of the test, after approximately 72 hours, and at test termination." Monsanto believes that alachlor data is appropriate and relevant analog data for CMA ecological endpoints.

The HPV registration number for Monsanto Company is : \_\_\_\_\_

Sincerely,

  
Clyde L. Livingston  
Chemical Regulatory Compliance  
Monsanto Company